

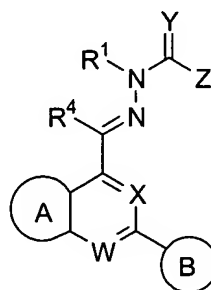
Appl. No. 10/004,287
Amdt. dated July 11, 2003
Reply to Office Action of March 11, 2003

PATENT

AMENDMENTS TO THE CLAIMS

Please cancel claims 2-5, 11, 31, 44-47, 53, 65-68, 74 and 92-101 without prejudice and amend claims 1, 6-9, 12-13, 22, 42-43, 54-55, 64, 69-72, 75-76 and 90-91 to read as follows. All claims pending, including those unchanged by the present amendment, are reproduced below for the convenience of the Examiner. This listing of claims will replace all prior versions, and listings, of claims in the application:

1. (Currently amended) A compound having the formula:



wherein

~~W and X are independently selected from the group consisting of N and CH;~~

W is N;

X is CH;

Y is selected from the group consisting of O, S and N(R);

wherein R is selected from the group consisting of H, CN, NO₂, (C₁-C₁₀)alkyl,

(C₃-C₁₀)cycloalkyl, (C₄-C₁₀)cycloalkyl-alkyl, (C₃-C₁₀)alkenyl and (C₂-

C₁₀)alkynyl;

Z is selected from the group consisting of H, (C₁-C₁₀)alkyl, (C₃-C₁₀)cycloalkyl, (C₄-

C₁₀)cycloalkyl-alkyl, (C₂-C₁₀)alkenyl, (C₂-C₁₀)alkynyl and NR²R³;

R¹, R² and R³ are independently selected from the group consisting of H, (C₁-C₁₀)alkyl,

(C₃-C₁₀)alkenyl, (C₂-C₁₀)alkynyl, (C₁-C₁₀)heteroalkyl, (C₃-C₁₀)cycloalkyl, (C₄-

C₁₀)cycloalkyl-alkyl, (C₃-C₁₀)cycloheteroalkyl-alkyl, (C₃-C₁₀)cycloheteroalkyl,

16 aryl, aryl(C₁-C₄)alkyl, aryl(C₁-C₄)heteroalkyl, heteroaryl(C₁-C₄)alkyl,
17 heteroaryl(C₁-C₄)heteroalkyl and perfluoro(C₁-C₆)alkyl; and wherein when Z is
18 NR²R³, R² and R³ can be combined to form a 5- to 7-membered heterocyclyl ring;
19 R⁴ is selected from the group consisting of H, (C₁-C₆)alkyl, (C₃-C₆)cycloalkyl, (C₄-
20 C₇)cycloalkyl-alkyl, (C₂-C₆)alkenyl and (C₂-C₆)alkynyl;

21 **A is a substituted or unsubstituted 6-membered fused carbocyclic or heterocyclic**
22 **aromatic ring system, wherein the heterocyclic aromatic ring system contains**
23 **1-2 N atoms; and**

24 ~~A is a substituted or unsubstituted fused carbocyclic or heterocyclic ring system,~~
25 ~~said ring system being mono- or bicyclic wherein said mono- or bicyclic rings~~
26 ~~are selected from the group consisting of five- and six-membered rings that~~
27 ~~are aromatic or partially or completely saturated; and~~

28 B is a substituted or unsubstituted five- or six-membered ring which is aromatic ~~or~~
29 ~~partially or completely saturated~~, containing at least one nitrogen atom, and
30 from 0 to 3 additional heteroatoms, wherein the B ring substituents are selected
31 from the group consisting of halogen, CF₃, CF₃O, (C₁-C₆)alkyl, perfluoro(C₁-
32 C₆)alkyl, (C₂-C₆)alkenyl, (C₂-C₆)alkynyl, (C₁-C₆)heteroalkyl, (C₁-C₆)alkoxy, (C₁-
33 C₆)thioalkoxy, amino, (C₁-C₆)alkylamino, di(C₁-C₆)alkylamino, (C₃-
34 C₁₀)cycloalkyl, (C₄-C₁₀)cycloalkyl-alkyl, (C₃-C₁₀)cycloheteroalkyl, cyano, nitro,
35 sulfonamido, (C₁-C₆)acyl, (C₁-C₆)acylamino, (C₁-C₆)alkoxycarbonyl, (C₁-
36 C₆)alkoxycarbonyl(C₁-C₆)alkyl, carboxamido and (C₁-C₆)heteroalkoxy.

1 2.-5. (Canceled)

1 6. (Currently amended) A compound of claim ~~2~~ 1, wherein Y is selected
2 from the group consisting of O and S.

1 7. (Currently amended) A compound of claim ~~2~~ 1, wherein Y is O.

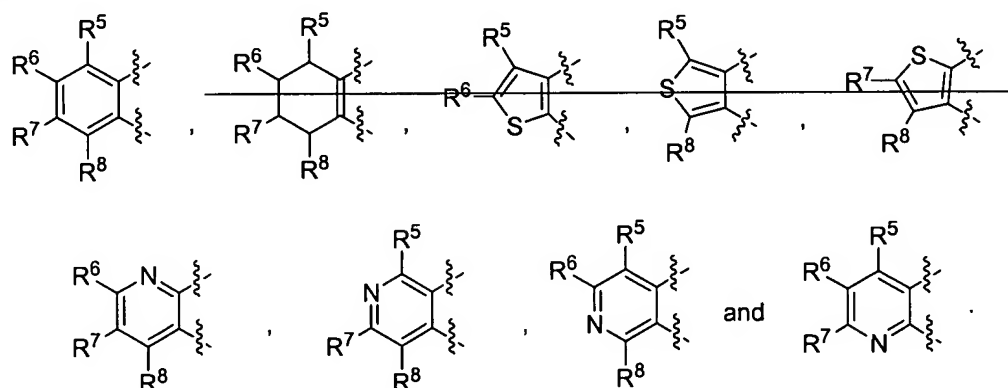
1 8. (Currently amended) A compound of claim ~~2~~ 1, wherein Y is S.

9. (Currently amended) A compound of claim ~~2~~ 1, wherein Z is NR^2R^3 .

10. (Original) A compound of claim 6, wherein R^4 is H.

11. (Canceled)

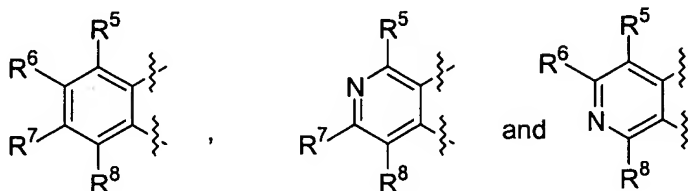
12. (Currently amended) A compound of claim 1, wherein A is selected from the group consisting of:



wherein

R^5 , R^6 , R^7 and R^8 are independently selected from the group consisting of H, halogen, CF_3 , $(\text{C}_1\text{-C}_6)\text{alkyl}$, $(\text{C}_2\text{-C}_6)\text{alkenyl}$, $(\text{C}_2\text{-C}_6)\text{alkynyl}$, $(\text{C}_1\text{-C}_6)\text{heteroalkyl}$, $(\text{C}_1\text{-C}_6)\text{alkoxy}$, $(\text{C}_1\text{-C}_6)\text{thioalkoxy}$, amino, $(\text{C}_1\text{-C}_6)\text{alkylamino}$, $\text{di}(\text{C}_1\text{-C}_6)\text{alkylamino}$, $(\text{C}_3\text{-C}_{10})\text{cycloalkyl}$, $(\text{C}_4\text{-C}_{10})\text{cycloalkyl-alkyl}$, $(\text{C}_3\text{-C}_{10})\text{cycloheteroalkyl}$, $(\text{C}_3\text{-C}_{10})\text{cycloheteroalkyl-alkyl}$, cyano, nitro, $(\text{C}_1\text{-C}_6)\text{acyl}$, $(\text{C}_1\text{-C}_6)\text{acylamino}$, $(\text{C}_1\text{-C}_6)\text{alkoxycarbonyl}$, $(\text{C}_1\text{-C}_6)\text{alkoxycarbonyl } (\text{C}_1\text{-C}_6)\text{alkyl}$, CONH_2 , $\text{CO-NH-}(\text{C}_1\text{-C}_6)\text{alkyl}$, $\text{CO-N}[(\text{C}_1\text{-C}_6)\text{alkyl}]_2$, SO_2NH_2 , $\text{SO}_2\text{NH-}(\text{C}_1\text{-C}_6)\text{alkyl}$, $\text{SO}_2\text{N-}[(\text{C}_1\text{-C}_6)\text{alkyl}]_2$ and $(\text{C}_1\text{-C}_6)\text{heteroalkoxy}$; or two adjacent R groups selected from R^5 , R^6 , R^7 and R^8 , can be linked together to form a new 5- or 6-membered carbocyclic or heterocyclic ring.

1 13. (Currently amended) A compound of claim 12, wherein ~~W is N; X is~~
2 ~~CH₃~~; Y is O or S; and A is selected from the group consisting of:



1 14. (Original) A compound of claim 1, wherein B contains a nitrogen atom at
2 a position two atoms away from the atom attaching B to the remainder of the molecule.

1 15. (Original) A compound of claim 1, wherein B contains a nitrogen atom at
2 the point of attachment of B to the remainder of the molecule.

1 16. (Original) A compound of claim 1, wherein B is selected from the group
2 consisting of 1-methylimidazol-5-yl, 1-(trifluoromethyl)imidazol-5-yl, 5-methylimidazol-1-yl, 5-
3 (trifluoromethyl)imidazol-1-yl, thiazol-5-yl, imidazol-1-yl, 1-methyl-1,3,4-triazolyl, and 4-
4 methyl-1,2,4-triazol-3-yl.

1 17. (Original) A compound of claim 1, wherein B is selected from the group
2 consisting of substituted or unsubstituted imidazolyl, substituted or unsubstituted thiazolyl and
3 substituted or unsubstituted triazolyl.

1 18. (Original) A compound of claim 13, wherein B contains a nitrogen atom
2 at a position two atoms away from the atom attaching B to the remainder of the molecule.

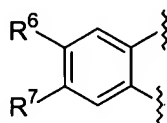
1 19. (Original) A compound of claim 13, wherein B contains a nitrogen atom
2 at the point of attachment of B to the remainder of the molecule.

1 20. (Original) A compound of claim 13, wherein B is selected from the group
2 consisting of 1-methylimidazol-5-yl, 1-(trifluoromethyl)imidazol-5-yl, 5-methylimidazol-1-yl, 5-

(trifluoromethyl)imidazol-1-yl, thiazol-5-yl, imidazol-1-yl, 1-methyl-1,3,4-triazolyl, and 4-methyl-1,2,4-triazol-3-yl.

21. (Original) A compound of claim 13, wherein B is selected from the group consisting of substituted or unsubstituted imidazolyl, substituted or unsubstituted thiazolyl and substituted or unsubstituted triazolyl.

22. (Currently amended) A compound of claim 1, wherein ~~W is N; X is CH~~; Y is O or S; Z is H, CH₃, NH₂ or NHCH₃; R¹ is H, (C₁-C₆)alkyl, (C₁-C₁₀)heteroalkyl, (C₄-C₁₀)cycloheteroalkyl-alkyl, (C₃-C₁₀)cycloheteroalkyl, aryl(C₁-C₄)alkyl, aryl(C₁-C₄)heteroalkyl, heteroaryl(C₁-C₄)alkyl, heteroaryl(C₁-C₄)heteroalkyl, or perfluoro(C₁-C₆)alkyl; R⁴ is H; A represents



wherein R⁶ and R⁷ are independently selected from the group consisting of H, halogen, CF₃, CF₃O, (C₁-C₄)alkyl, (C₂-C₄)alkenyl, (C₂-C₄)alkynyl, (C₁-C₄)heteroalkyl, (C₃-C₁₀)cycloheteroalkyl-alkyl and cyano; and B is a five-membered aromatic ring system containing at least one nitrogen atom.

23. (Original) A compound of claim 22, wherein Y is S.

24. (Original) A compound of claim 22, wherein Z is NR²R³.

25. (Original) A compound of claim 22, wherein Z is NH₂.

26. (Original) A compound of claim 22, wherein R¹ is (C₁-C₆)alkyl, (C₁-C₆)heteroalkyl or (C₃-C₁₀)cycloheteroalkyl-alkyl.

27. (Original) A compound of claim 22, wherein B is a five-membered aromatic ring system containing 1-2 nitrogen atoms and 0-1 sulfur atoms.

1 **28.** (Original) A compound of claim 27, wherein B is unsubstituted or
2 substituted by (C₁-C₃)alkyl, CF₃, cyano, or halogen.

1 **29.** (Original) A compound of claim 22, wherein Z is NH₂; R⁶ is selected
2 from the group consisting of H, halogen, CF₃, CF₃O, (C₁-C₄)alkyl, (C₂-C₄)alkenyl, (C₁-
3 C₄)heteroalkyl, (C₃-C₁₀)cycloheteroalkyl-alkyl and cyano, wherein the alkyl, alkenyl and
4 heteroalkyl groups optionally bear additional substituents selected from cyano, carboxamido, (C₁-
5 C₃)alkylsulfonyl or (C₁-C₃)alkoxy; and R⁷ is selected from the group consisting of H, halogen,
6 CF₃, CF₃O, (C₁-C₄)alkyl, (C₂-C₄)alkenyl, (C₂-C₄)alkynyl, (C₁-C₄)heteroalkyl and cyano.

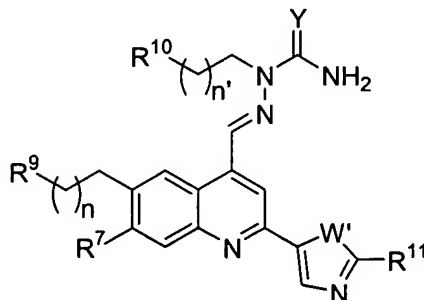
1 **30.** (Original) A compound of claim 29, wherein R⁶ is selected from the
2 group consisting of CH₂(CH₂)_mCN, CH₂(CH₂)_nSO₂CH₃ and CH₂(CH₂)_nOCH₃, wherein the
3 subscript n is an integer from 0 to 2.

1 **31.** (Canceled)

1 **32.** (Original) A compound of claim 29, wherein R⁷ is selected from H,
2 halogen, CF₃ and (C₁-C₄)alkyl.

1 **33.** (Original) A compound of claim 29, wherein R⁷ is methyl.

1 **34.** (Original) A compound of claim 1, having the formula:



2 wherein Y is O, S or N-CN; W' is N(CH₃), N(CF₃), N(CH₂CH₃), O or S; the subscripts n
3 and n' are independently integers from 0 to 3; R⁷ is H, halogen, CF₃, CF₃O, (C₁-
4 C₄)alkyl, (C₂-C₄)alkenyl, (C₂-C₄)alkynyl, (C₁-C₄)heteroalkyl or cyano; R⁹ is CN,
5

6 CONH₂, CO-NH-(C₁-C₆)alkyl, CO-N[(C₁-C₆)alkyl]₂, CO-NH-(C₁-C₆)heteroalkyl,
7 CO-N[(C₁-C₆)heteroalkyl]₂, S(O)_{n''}-(C₁-C₆)alkyl, S(O)_{n''}-(C₁-C₆)heteroalkyl,
8 heteroaryl, (C₁-C₆)alkoxy or (C₃-C₆)cycloheteroalkyl, wherein each n'' is
9 independently an integer of 0 to 2; R¹⁰ is NH₂, NH-(C₁-C₆)alkyl, N[(C₁-
10 C₆)alkyl]₂, NH-(C₁-C₆)heteroalkyl, N[(C₁-C₆)heteroalkyl]₂, (C₁-C₆)heteroalkyl,
11 S(O)_{n''}-(C₁-C₆)alkyl, S(O)_{n''}-(C₁-C₆)heteroalkyl, aryl, heteroaryl, O-(C₁-C₆)alkyl,
12 O-(C₁-C₆)heteroalkyl or (C₃-C₈)cycloheteroalkyl; and R¹¹ is H, CF₃, NH₂, NH-
13 (C₁-C₆)alkyl, N[(C₁-C₆)alkyl]₂, halogen or (C₁-C₃)alkyl.

A' 1 35. (Original) A compound of claim 34, wherein Y is O or S; W' is N-CH₃; n
2 is 2; n' is 1-3; R⁹ is cyano, CONH₂, SO₂-(C₁-C₆)alkyl, (C₁-C₆)alkoxy or (C₃-C₆)cycloheteroalkyl;
3 R¹⁰ is NH-(C₁-C₆)alkyl, N[(C₁-C₆)alkyl]₂, NH-(C₁-C₆)heteroalkyl, N[(C₁-C₆)heteroalkyl]₂, O-
4 (C₁-C₆)alkyl, O-(C₁-C₆)heteroalkyl, (C₁-C₆)alkoxy or (C₃-C₈)cycloheteroalkyl; and R¹¹ is H.

1 36. (Original) A compound of claim 22, wherein B contains a nitrogen atom
2 at a position two atoms away from the atom attaching B to the remainder of the molecule.

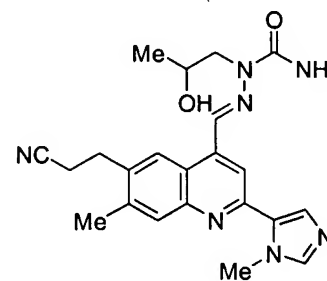
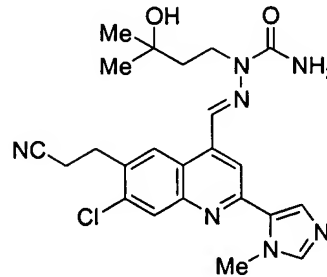
1 37. (Original) A compound of claim 22, wherein B contains a nitrogen atom
2 at the point of attachment of B to the remainder of the molecule.

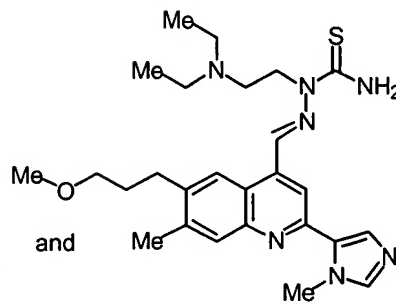
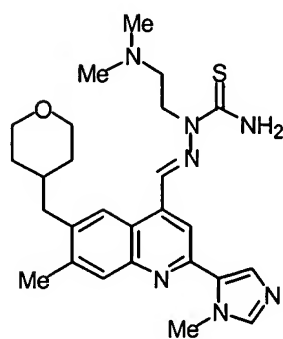
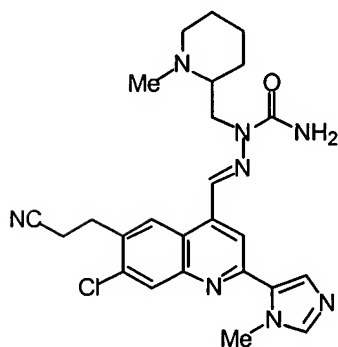
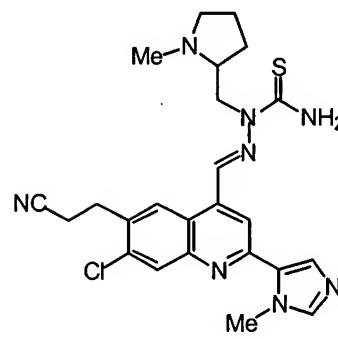
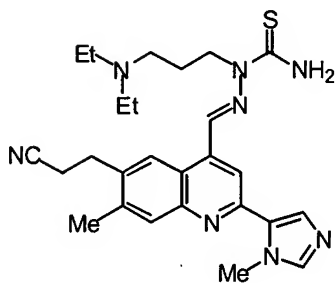
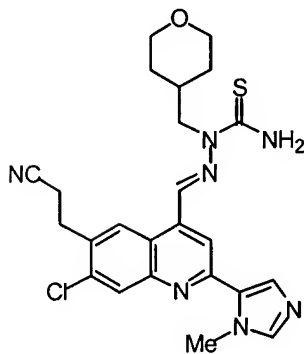
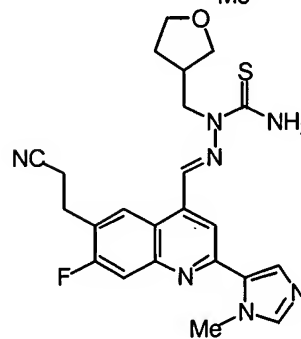
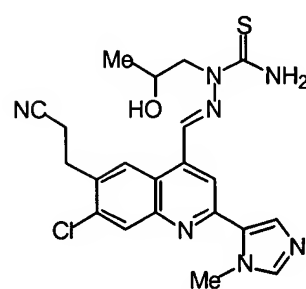
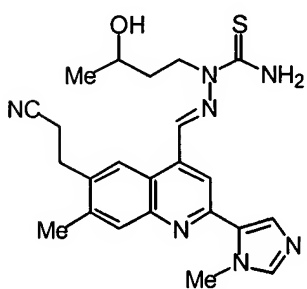
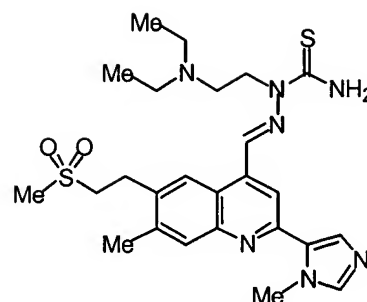
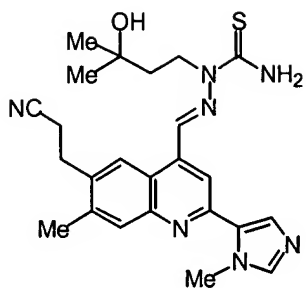
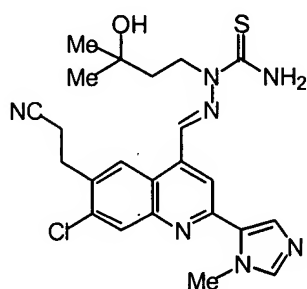
1 38. (Original) A compound of claim 22, wherein B is selected from the group
2 consisting of substituted or unsubstituted imidazolyl, substituted or unsubstituted thiazolyl and
3 substituted or unsubstituted triazolyl.

1 39. (Original) A compound of claim 22, wherein B is selected from the group
2 consisting of 1-methylimidazol-5-yl, 1-(trifluoromethyl)imidazol-5-yl, 5-methylimidazol-1-yl, 5-
3 (trifluoromethyl)imidazol-1-yl, thiazol-5-yl, imidazol-1-yl, 1-methyl-1,3,4-triazolyl, and 4-
4 methyl-1,2,4-triazol-3-yl.

1 40. (Original) A compound of claim 1, wherein Y is S; Z is NH₂ and R¹ is
2 (C₁-C₆)alkyl.

42. (Currently amended) A compound of claim 1, wherein said compound is the group consisting of:

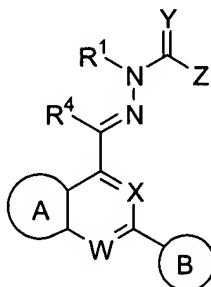




and

A'

43. (Currently amended) A composition comprising a pharmaceutically acceptable excipient and a compound having the formula:



wherein

~~W and X are independently selected from the group consisting of N and CH;~~

W is N;

X is CH;

Y is selected from the group consisting of O, S and N(R);

wherein R is selected from the group consisting of H, CN, NO₂, (C₁-C₁₀)alkyl, (C₃-C₁₀)cycloalkyl, (C₄-C₁₀)cycloalkyl-alkyl, (C₃-C₁₀)alkenyl and (C₂-C₁₀)alkynyl;

Z is selected from the group consisting of H, (C₁-C₁₀)alkyl, (C₃-C₁₀)cycloalkyl, (C₄-C₁₀)cycloalkyl-alkyl, (C₂-C₁₀)alkenyl, (C₂-C₁₀)alkynyl and NR²R³;

R¹, R² and R³ are independently selected from the group consisting of H, (C₁-C₁₀)alkyl, (C₃-C₁₀)alkenyl, (C₂-C₁₀)alkynyl, (C₂-C₁₀)heteroalkyl, (C₃-C₁₀)cycloalkyl, (C₄-C₁₀)cycloalkyl-alkyl, (C₃-C₁₀)cycloheteroalkyl-alkyl, (C₃-C₁₀)cycloheteroalkyl, aryl, aryl(C₁-C₄)alkyl, aryl(C₂-C₄)heteroalkyl, heteroaryl(C₂-C₄)alkyl, heteroaryl(C₂-C₄)heteroalkyl and perfluoro(C₁-C₆)alkyl; and wherein when Z is NR²R³, R² and R³ can be combined to form a 5- to 7-membered ring; and wherein when Y is N(R), R and R¹ are optionally combined to form a 5- to 7-membered ring;

R⁴ is selected from the group consisting of H, (C₁-C₆)alkyl, (C₃-C₆)cycloalkyl, (C₄-C₇)cycloalkyl-alkyl, (C₂-C₆)alkenyl and (C₂-C₆)alkynyl;

24 **A is a substituted or unsubstituted 6-membered fused carbocyclic or heterocyclic**
25 **aromatic ring system, wherein the heterocyclic aromatic ring system contains**
26 **1-2 N atoms; and**

27 ~~**A is a substituted or unsubstituted fused carbocyclic or heterocyclic ring system,**~~
28 ~~**said ring system being mono- or bicyclic wherein said mono- or bicyclic rings**~~
29 ~~**are selected from the group consisting of five- and six-membered rings that**~~
30 ~~**are aromatic or partially or completely saturated; and**~~

31 B is a substituted or unsubstituted five- or six-membered ring which is aromatic ~~or~~
32 ~~**partially or completely saturated**~~, containing at least one nitrogen atom, and
33 from 0 to 3 additional heteroatoms, wherein the B ring substituents are selected
34 from the group consisting of halogen, CF₃, CF₃O, (C₁-C₆)alkyl, perfluoro(C₁-
35 C₆)alkyl, (C₂-C₆)alkenyl, (C₂-C₆)alkynyl, (C₁-C₆)heteroalkyl, (C₁-C₆)alkoxy, (C₁-
36 C₆)thioalkoxy, amino, (C₁-C₆)alkylamino, di(C₁-C₆)alkylamino, (C₃-
37 C₁₀)cycloalkyl, (C₄-C₁₀)cycloalkyl-alkyl, (C₃-C₁₀)cycloheteroalkyl, cyano, nitro,
38 sulfonamido, (C₁-C₆)acyl, (C₁-C₆)acylamino, (C₂-C₆)alkoxycarbonyl, (C₂-
39 C₆)alkoxycarbonyl(C₁-C₆)alkyl, carboxamido and (C₁-C₆)heteroalkoxy.

1 **44.-47. (Canceled)**

1 **48. (Original) A composition in accordance with claim 43, wherein Y is**
2 **selected from the group consisting of O and S.**

1 **49. (Original) A composition in accordance claim 43, wherein Y is O.**

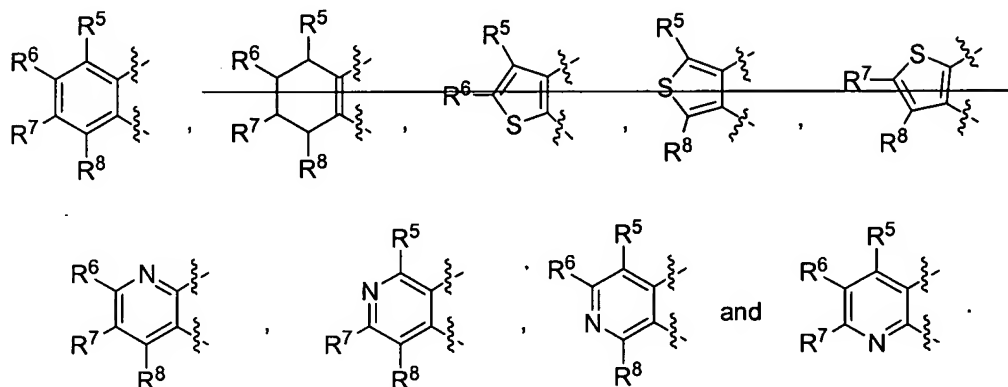
1 **50. (Original) A composition in accordance claim 43, wherein Y is S.**

1 **51. (Original) A composition in accordance claim 43, wherein Z is NR²R³.**

1 **52. (Original) A composition in accordance with claim 48, wherein R⁴ is H.**

1 **53. (Canceled)**

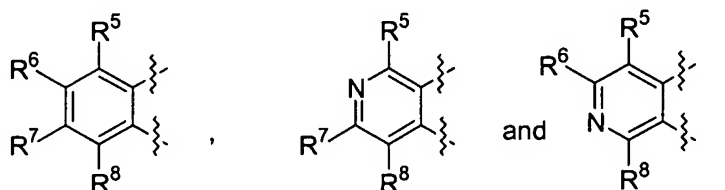
- 1 **54.** (Currently amended) A composition in accordance with claim **43**,
2 wherein A is selected from the group consisting of:



wherein

A1
R⁵, R⁶, R⁷ and R⁸ are independently selected from the group consisting of H, halogen, CF₃, (C₁-C₆)alkyl, (C₂-C₆)alkenyl, (C₂-C₆)alkynyl, (C₁-C₆)heteroalkyl, (C₁-C₆)alkoxy, (C₁-C₆)thioalkoxy, amino, (C₁-C₆)alkylamino, di(C₁-C₆)alkylamino, (C₃-C₁₀)cycloalkyl, (C₄-C₁₀)cycloalkyl-alkyl, (C₃-C₁₀)cycloheteroalkyl, (C₃-C₁₀)cycloheteroalkyl-alkyl, cyano, nitro, (C₁-C₆)acyl, (C₁-C₆)acylamino, (C₂-C₆)alkoxycarbonyl, (C₃-C₆)alkoxycarbonylalkyl, CONH₂, CO-NH-(C₁-C₆)alkyl, CO-N[(C₁-C₆)alkyl]₂, SO₂NH₂, SO₂NH-(C₁-C₆)alkyl, SO₂N-[(C₁-C₆)alkyl]₂ and (C₁-C₆)heteroalkoxy; or two adjacent R groups can be linked together to form a new 5- or 6-membered carbocyclic or heterocyclic ring.

- 1 **55.** (Currently amended) A composition in accordance with claim **43**,
2 wherein ~~W is N; X is CH~~; Y is O or S; and A is selected from the group consisting of:



1 **56.** (Original) A composition in accordance with claim **43**, wherein B
2 contains a nitrogen atom at a position two atoms away from the atom attaching B to the
3 remainder of the molecule.

1 **57.** (Original) A composition in accordance with claim **43**, wherein B
2 contains a nitrogen atom at the point of attachment of B to the remainder of the molecule.

1 **58.** (Original) A composition in accordance with claim **43**, wherein B is
2 selected from the group consisting of 1-methylimidazol-5-yl, 1-(trifluoromethyl)imidazol-5-yl,
3 5-methylimidazol-1-yl, 5-(trifluoromethyl)imidazol-1-yl, thiazol-5-yl, imidazol-1-yl, 1-methyl-
4 1,3,4-triazolyl, and 4-methyl-1,2,4-triazol-3-yl.

A1

1 **59.** (Original) A composition in accordance with claim **43**, wherein B is
2 selected from the group consisting of substituted or unsubstituted imidazolyl, substituted or
3 unsubstituted thiazolyl and substituted or unsubstituted triazolyl.

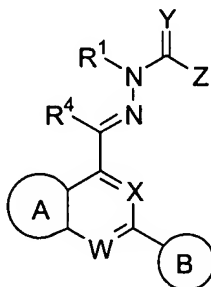
1 **60.** (Original) A composition in accordance with claim **55**, wherein B
2 contains a nitrogen atom at a position two atoms away from the atom attaching B to the
3 remainder of the molecule.

1 **61.** (Original) A composition in accordance with claim **55**, wherein B
2 contains a nitrogen atom at the point of attachment of B to the remainder of the molecule.

1 **62.** (Original) A composition in accordance with claim **55**, wherein B is
2 selected from the group consisting of 1-methylimidazol-5-yl, 1-(trifluoromethyl)imidazol-5-yl,
3 5-methylimidazol-1-yl, 5-(trifluoromethyl)imidazol-1-yl, thiazol-5-yl, imidazol-1-yl, 1-methyl-
4 1,3,4-triazolyl, and 4-methyl-1,2,4-triazol-3-yl.

1 **63.** (Original) A composition in accordance with claim **55**, wherein B is
2 selected from the group consisting of substituted or unsubstituted imidazolyl, substituted or
3 unsubstituted thiazolyl and substituted or unsubstituted triazolyl.

64. (Currently amended) A method for treating an inflammatory, ~~metabolic~~
~~or malignant~~ condition or cancer, said method comprising administering to a subject in need of
such treatment, an effective amount of a compound having the formula:



wherein

~~W and X are independently selected from the group consisting of N and CH;~~

W is N;

X is CH;

Y is selected from the group consisting of O, S and N(R);

wherein R is selected from the group consisting of H, CN, NO₂, (C₁-C₁₀)alkyl,
(C₃-C₁₀)cycloalkyl, (C₄-C₁₀)cycloalkyl-alkyl, (C₃-C₁₀)alkenyl and (C₂-
C₁₀)alkynyl;

Z is selected from the group consisting of H, (C₁-C₁₀)alkyl, (C₃-C₁₀)cycloalkyl, (C₄-
C₁₀)cycloalkyl-alkyl, (C₂-C₁₀)alkenyl, (C₂-C₁₀)alkynyl and NR²R³;

R¹, R² and R³ are independently selected from the group consisting of H, (C₁-C₁₀)alkyl,
(C₃-C₁₀)alkenyl, (C₂-C₁₀)alkynyl, (C₂-C₁₀)heteroalkyl, (C₃-C₁₀)cycloalkyl, (C₄-
C₁₀)cycloalkyl-alkyl, (C₃-C₁₀)cycloheteroalkyl-alkyl, (C₃-C₁₀)cycloheteroalkyl,
aryl, aryl(C₁-C₄)alkyl, aryl(C₂-C₄)heteroalkyl, heteroaryl(C₂-C₄)alkyl,
heteroaryl(C₂-C₄)heteroalkyl and perfluoro(C₁-C₆)alkyl; and wherein when Z is
NR²R³, R² and R³ can be combined to form a 5- to 7-membered ring; and wherein
when Y is N(R), R and R¹ are optionally combined to form a 5- to 7-membered
ring;

R⁴ is selected from the group consisting of H, (C₁-C₆)alkyl, (C₃-C₆)cycloalkyl, (C₄-C₇)cycloalkyl-alkyl, (C₂-C₆)alkenyl and (C₂-C₆)alkynyl;

A is a substituted or unsubstituted 6-membered fused carbocyclic or heterocyclic aromatic ring system, wherein the heterocyclic aromatic ring system contains 1-2 N atoms; and

~~A is a substituted or unsubstituted fused carbocyclic or heterocyclic ring system, said ring system being mono- or bicyclic wherein said mono- or bicyclic rings are selected from the group consisting of five- and six-membered rings that are aromatic or partially or completely saturated; and~~

B is a substituted or unsubstituted five- or six-membered ring which is aromatic ~~or partially or completely saturated~~, containing at least one nitrogen atom, and from 0 to 3 additional heteroatoms, wherein the B ring substituents are selected from the group consisting of halogen, CF₃, CF₃O, (C₁-C₆)alkyl, perfluoro(C₁-C₆)alkyl, (C₂-C₆)alkenyl, (C₂-C₆)alkynyl, (C₁-C₆)heteroalkyl, (C₁-C₆)alkoxy, (C₁-C₆)thioalkoxy, amino, (C₁-C₆)alkylamino, di(C₁-C₆)alkylamino, (C₃-C₁₀)cycloalkyl, (C₄-C₁₀)cycloalkyl-alkyl, (C₃-C₁₀)cycloheteroalkyl, cyano, nitro, sulfonamido, (C₁-C₆)acyl, (C₁-C₆)acylamino, (C₂-C₆)alkoxycarbonyl, (C₂-C₆)alkoxycarbonyl(C₁-C₆)alkyl, carboxamido and (C₁-C₆)heteroalkoxy.

65.-68. (Canceled)

69. (Currently amended) A method in accordance with claim ~~65~~ 64, wherein

Y is selected from the group consisting of O and S.

70. (Currently amended) A method in accordance with claim ~~65~~ 64, wherein

Y is O.

71. (Currently amended) A method in accordance with claim ~~65~~ 64, wherein

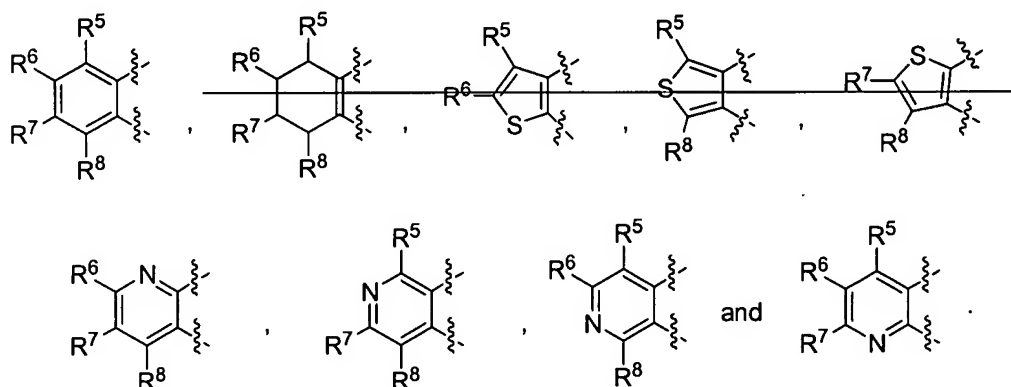
Y is S.

72. (Currently amended) A method in accordance with claim ~~65~~ 64, wherein
Z is NR^2R^3 .

73. (Original) A method in accordance with claim 69, wherein R^4 is H.

74. (Canceled)

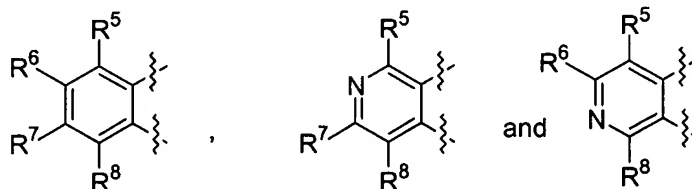
75. (Currently amended) A method in accordance with claim 64, wherein A is
selected from the group consisting of:



wherein

R^5 , R^6 , R^7 and R^8 are independently selected from the group consisting of H, halogen, CF_3 , $(\text{C}_1\text{-C}_6)\text{alkyl}$, $(\text{C}_2\text{-C}_6)\text{alkenyl}$, $(\text{C}_2\text{-C}_6)\text{alkynyl}$, $(\text{C}_1\text{-C}_6)\text{heteroalkyl}$, $(\text{C}_1\text{-C}_6)\text{alkoxy}$, $(\text{C}_1\text{-C}_6)\text{thioalkoxy}$, amino, $(\text{C}_1\text{-C}_6)\text{alkylamino}$, $\text{di}(\text{C}_1\text{-C}_6)\text{alkylamino}$, $(\text{C}_3\text{-C}_{10})\text{cycloalkyl}$, $(\text{C}_4\text{-C}_{10})\text{cycloalkyl-alkyl}$, $(\text{C}_3\text{-C}_{10})\text{cycloheteroalkyl}$, $(\text{C}_3\text{-C}_{10})\text{cycloheteroalkyl-alkyl}$, cyano, nitro, $(\text{C}_1\text{-C}_6)\text{acyl}$, $(\text{C}_1\text{-C}_6)\text{acylamino}$, $(\text{C}_2\text{-C}_6)\text{alkoxycarbonyl}$, $(\text{C}_3\text{-C}_6)\text{alkoxycarbonylalkyl}$, CONH_2 , $\text{CO-NH-(C}_1\text{-C}_6)\text{alkyl}$, $\text{CO-N}[(\text{C}_1\text{-C}_6)\text{alkyl}]_2$, SO_2NH_2 , $\text{SO}_2\text{NH-(C}_1\text{-C}_6)\text{alkyl}$, $\text{SO}_2\text{N}[(\text{C}_1\text{-C}_6)\text{alkyl}]_2$ and $(\text{C}_1\text{-C}_6)\text{heteroalkoxy}$; or two adjacent R groups can be linked together to form a new 5- or 6-membered carbocyclic or heterocyclic ring.

1 76. (Currently amended) A method in accordance with claim 64, wherein ~~W~~
2 ~~is N; X is CH~~; Y is O or S; and A is selected from the group consisting of:



1 77. (Original) A method in accordance with claim 64, wherein B contains a
2 nitrogen atom at a position two atoms away from the atom attaching B to the remainder of the
3 molecule.

AI 1 78. (Original) A method in accordance with claim 64, wherein B contains a
2 nitrogen atom at the point of attachment of B to the remainder of the molecule.

1 79. (Original) A method in accordance with claim 64, wherein B is selected
2 from the group consisting of 1-methylimidazol-5-yl, 1-(trifluoromethyl)imidazol-5-yl, 5-
3 methylimidazol-1-yl, 5-(trifluoromethyl)imidazol-1-yl, thiazol-5-yl, imidazol-1-yl, 1-methyl-
4 1,3,4-triazolyl, and 4-methyl-1,2,4-triazol-3-yl.

1 80. (Original) A method in accordance with claim 64, wherein B is selected
2 from the group consisting of substituted or unsubstituted imidazolyl, substituted or unsubstituted
3 thiazolyl and substituted or unsubstituted triazolyl.

1 81. (Original) A method in accordance with claim 76, wherein B contains a
2 nitrogen atom at a position two atoms away from the atom attaching B to the remainder of the
3 molecule.

1 82. (Original) A method in accordance with claim 76, wherein B contains a
2 nitrogen atom at the point of attachment of B to the remainder of the molecule.

1 **83.** (Original) A method in accordance with claim **76**, wherein B is selected
2 from the group consisting of 1-methylimidazol-5-yl, 1-(trifluoromethyl)imidazol-5-yl, 5-
3 methylimidazol-1-yl, 5-(trifluoromethyl)imidazol-1-yl, thiazol-5-yl, imidazol-1-yl, 1-methyl-
4 1,3,4-triazolyl, and 4-methyl-1,2,4-triazol-3-yl.

1 **84.** (Original) A method in accordance with claim **76**, wherein B is selected
2 from the group consisting of substituted or unsubstituted imidazolyl, substituted or unsubstituted
3 thiazolyl and substituted or unsubstituted triazolyl.

1 **85.** (Original) A method in accordance with claim **64**, wherein said
2 compound is administered orally.

AI 1 **86.** (Original) A method in accordance with claim **64**, wherein said
2 compound is administered topically.

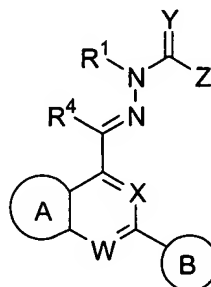
1 **87.** (Original) A method in accordance with claim **64**, wherein said
2 compound is administered intravenously or intramuscularly.

1 **88.** (Original) A method in accordance with claim **64**, wherein said
2 compound is administered in combination with a second therapeutic agent, said second
3 therapeutic agent being a member selected from the group consisting of prednisone,
4 dexamethasone, beclomethasone, methylprednisone, betamethasone, hydrocortisone,
5 methotrexate, cyclosporin, rapamycin, tacrolimus, antihistamine drugs, TNF antibodies, IL-1
6 antibodies, soluble TNF receptors, soluble IL-1 receptors, TNF or IL-1 receptor antagonists, non-
7 steroidal antiinflammatory agents, COX-2 inhibitors, antidiabetic agents, and anticancer agents.

1 **89.** (Original) A method in accordance with claim **88**, wherein said
2 administering is sequential.

1 90. (Currently amended) A method in accordance with claim 64, wherein said
2 inflammatory, ~~metabolic or malignant~~ condition is selected from the group consisting of
3 rheumatoid arthritis, inflammatory bowel disease, psoriasis, ~~cancer~~, diabetes and septic shock.

1 91. (Currently amended) A method for treating a condition or disorder
2 mediated by IKK, wherein the condition or disorder is selected from the group consisting of
3 an inflammatory condition and cancer, comprising
4 administering to a subject in need thereof a therapeutically effective amount of a
5 compound having the formula:



6 wherein
7
8 ~~W and X are independently selected from the group consisting of N and CH;~~
9 W is N;
10 X is CH;
11 Y is selected from the group consisting of O, S and N(R);
12 wherein R is selected from the group consisting of H, CN, NO₂, (C₁-C₁₀)alkyl,
13 (C₃-C₁₀)cycloalkyl, (C₄-C₁₀)cycloalkyl-alkyl, (C₃-C₁₀)alkenyl and (C₂-
14 C₁₀)alkynyl;
15 Z is selected from the group consisting of H, (C₁-C₁₀)alkyl, (C₃-C₁₀)cycloalkyl, (C₄-
16 C₁₀)cycloalkyl-alkyl, (C₂-C₁₀)alkenyl, (C₂-C₁₀)alkynyl and NR²R³;
17 R¹, R² and R³ are independently selected from the group consisting of H, (C₁-C₁₀)alkyl,
18 (C₃-C₁₀)alkenyl, (C₂-C₁₀)alkynyl, (C₁-C₁₀)heteroalkyl, (C₃-C₁₀)cycloalkyl, (C₄-
19 C₁₀)cycloalkyl-alkyl, (C₃-C₁₀)cycloheteroalkyl-alkyl, (C₃-C₁₀)cycloheteroalkyl,
20 aryl, aryl(C₁-C₄)alkyl, aryl(C₁-C₄)heteroalkyl, heteroaryl(C₁-C₄)alkyl,

21 heteroaryl(C₁-C₄)heteroalkyl and perfluoro(C₁-C₆)alkyl; and wherein when Z is
22 NR²R³, R² and R³ can be combined to form a 5- to 7-membered heterocyclyl ring;
23 R⁴ is selected from the group consisting of H, (C₁-C₆)alkyl, (C₃-C₆)cycloalkyl, (C₄-
24 C₇)cycloalkyl-alkyl, (C₂-C₆)alkenyl and (C₂-C₆)alkynyl;

25 **A is a substituted or unsubstituted 6-membered fused carbocyclic or heterocyclic**
26 **aromatic ring system, wherein the heterocyclic aromatic ring system contains**
27 **1-2 N atoms; and**

28 ~~**A is a substituted or unsubstituted fused carbocyclic or heterocyclic ring system,**~~
29 ~~**said ring system being mono- or bicyclic wherein said mono- or bicyclic rings**~~
30 ~~**are selected from the group consisting of five- and six-membered rings that**~~
31 ~~**are aromatic or partially or completely saturated; and**~~

32 B is a substituted or unsubstituted five- or six-membered ring which is aromatic ~~or~~
33 ~~**partially or completely saturated**~~, containing at least one nitrogen atom, and
34 from 0 to 3 additional heteroatoms, wherein the B ring substituents are selected
35 from the group consisting of halogen, CF₃, CF₃O, (C₁-C₆)alkyl, perfluoro(C₁-
36 C₆)alkyl, (C₂-C₆)alkenyl, (C₂-C₆)alkynyl, (C₁-C₆)heteroalkyl, (C₁-C₆)alkoxy, (C₁-
37 C₆)thioalkoxy, amino, (C₁-C₆)alkylamino, di(C₁-C₆)alkylamino, (C₃-
38 C₁₀)cycloalkyl, (C₄-C₁₀)cycloalkyl-alkyl, (C₃-C₁₀)cycloheteroalkyl, cyano, nitro,
39 sulfonamido, (C₁-C₆)acyl, (C₁-C₆)acylamino, (C₁-C₆)alkoxycarbonyl, (C₁-
40 C₆)alkoxycarbonyl(C₁-C₆)alkyl, carboxamido and (C₁-C₆)heteroalkoxy.

1 **92. -101. (Canceled)**